SERUM LEVELS OF GONADOTROPINS DURING LACTATIONAL AMENORRHOEA

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Introduction

Although a few studies have been reported about patterns of circulating pituitary gonadotropins during lactational amenorrhoea, the basic physiology of lactational amenorrhoea is not yet clearly understood. Available evidence (Keller, 1968; Zarate *et al,* 1972) suggests that ovarian refractoriness might be one of the important factors for anovulation and amenorrhoea. (Kettel and Bradbury, 1961; Crystle *et al,* 1970; Forbes *et al,* 1954) observed that pituitary FSH and LH levels measured in plasma and urine varied from those observed during the normal menstrual cycle. On the other hand, Johnsen and Fuchs demonstrated that there is no significant difference in excretion of total gonadotropin activity during lactation and in the menstrual cycle.

Whether prolactin plays any role in inhibiting pituitary release of LH and FSH in the puerperium has not yet been elucidated. Jaffe *et al,* (1969-1973) reported that analyses of sera over 120 days during lactation showed an association of elevated prolactin levels and decreased gonadotropins (FSH and LH). Following weaning, prolactin concentration decreased and ovulation occurred as manifested by the surge of FSH and LH and subsequent menses. However, these investigators did observe that the baseline levels were variable with numerous peaks. Thus, the studies reported in the literature about the relationship between the pituitary hormonal levels and the lactational amenorrhoea are not conclusive.

The aim of the present study was to investigate whether the changes in the circulating pattern of FSH, LH and prolactin were responsible for amenorrhoea.

Material and Methods

Serial estimations of FSH, LH and prolactin were carried out in 9 patients with lactational amenorrhoea. Vaginal cytology was done whenever possible. Three of the 9 mothers included in this study complained of poor lactation and were giving bottle feeds in addition to breast feeding. All others had no complaints regarding lactation.

Five patients study commenced within 1½ months from the last delivery. Others were studied 3 months, 9 months, 12

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months and 15 months respectively after the last parturition. The day of the first blood collection was considered as Day 1. Blood samples were drawn from antecubital vein during the first visit and then every 4 days after the first visit.

The blood samples were allowed to clot and serum was separated and it was frozen and kept at a constant temperature of —20°C. Serum FSH, LH and prolactin were measured by the radioimmunoassay technique of Medgley (1966, 1967). All the samples from an individual subject were analyzed in the same assay. The second reference preparation of Human Menopausal Gonadotropin (2 IRP) was used as the standard for FSH and LH. In our laboratory, the lower limit of sensitivity for the FSH and LH assay is 1 mIU/ml and 0.5 mIU/ml respectively.

Results

The mean levels of FSH, LH and prolactin of the five patients in whom the study commenced within one and half months after delivery are given in Table 1 and Graph—I.

The serum values of FSH ranged from 1 to 18 mIU/ml. There was no FSH peak in any of these women.

The levels of LH in this series ranged from 5-29 mIU/ml and serum prolactin values varied from 28-287 ng/ml. There was no significant difference in hormonal levels in four successful lactators and one comparatively poor lactator who required twice a day bottle feeding for the baby.

The vaginal cytology was studied in 4 of these 5 patients intermittently. The smears were considered atrophic when there were 10-20% or more parabasal cells seen. The karyopyknotic index was below 10% and only one patient had the karyopyknotic index going upto 20%. Only one patient had a KPI index of 40% on 28th day of study but this was not followed by menstruation and was not associated with a definite FSH or LH peak during the study interval.

Graph—II shows hormonal levels of FSH, LH and prolactin in normally menstruating women.

TABLE 1

Mean Values of FSH, LH and Prolactin in 4 Successfully Lactating Women Within and One and Half Months From the Last Delivery

	No. of Patients studied	Day of blood collection	Mean Value		
			FESH mIU/ml	LH mIU/ml	Prolactin ng/ml
	4	1st Day	84.72	24.12	104.0
	4	4th Day	9.90	17.5	96.0
	3	8th Day	8.96	13.6	139.6
	2	12th Day	6.98	17.1	74.5
One to one and	2	16th Day	11.85	9.75	69.5
half months	2	20th Day	9.93	16.0	69.0
after delivery	2	24th Day	16.0	24.25	181.5
	1	28th Day	2.50	27.0	105.0
	2	32nd Day	7.95	12.5	85.25
	1	36th Day	3.23	26.5	88.0
	2	40th Day	4.33	17.25	135.0
	1	48th Day	6.33	17.0	97.0

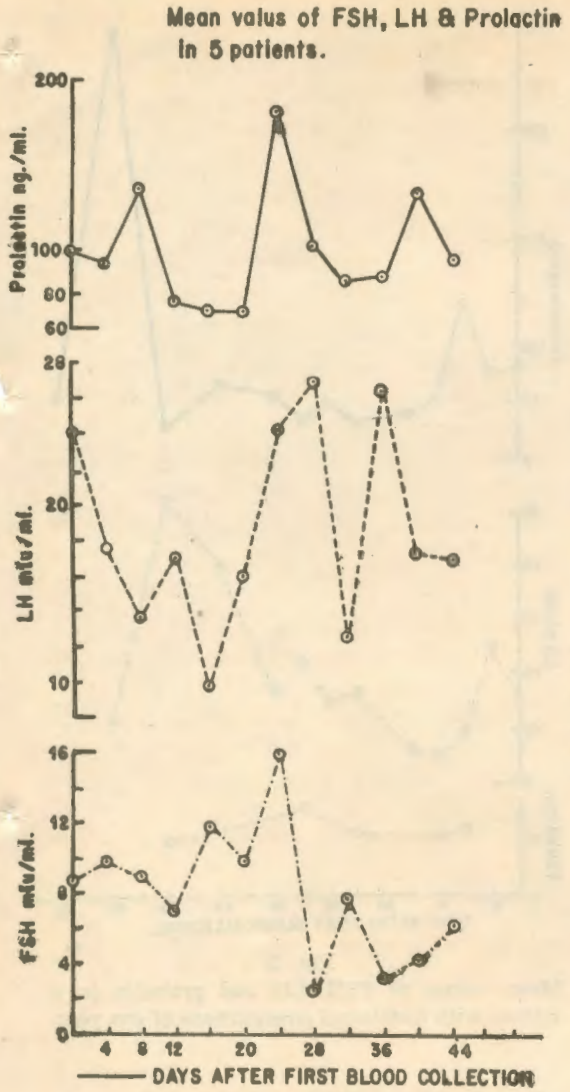

Fig. 1
Mean value of FSH, LH and prolactin in 5 patients delivered 4 to 6 weeks back.

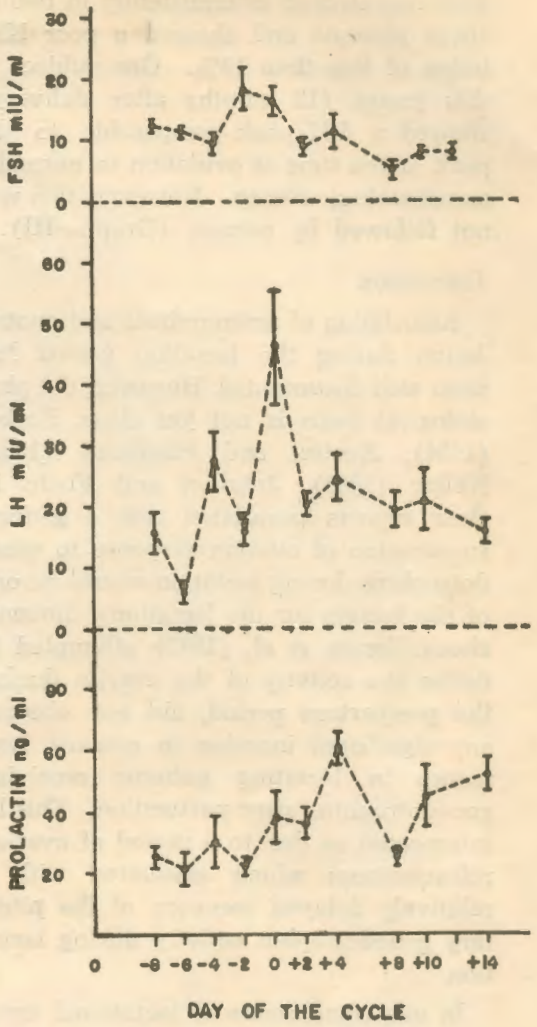

Fig. 2
Mean values of FSH, LH and prolactin in normal menstrual cycle.

One patient was studied at 3 months after the last delivery. She was giving 3-4 bottle feedings in addition to breast feeding. Her FSH values ranged from 1.88 to 8.4 mIU/ml, LH levels varied from 2.5 to 14 mIU/ml and prolactin values appeared comparatively lower. Vaginal cytology showed a poor KPI index.

Three women were studied at 9, 12 and 15 months respectively after the parturition. Their FSH levels ranged from 2.6 to 16 mIU/ml, LH levels ranged from 5.5 to 52 mIU/ml and the prolactin values ranged from 11.5 to 390 ng/ml. There was not much difference in hormonal levels in two good lactators compared to one pa-

tient complaining of poor lactation. Cytology was studied intermittently in two of these patients and showed a poor KPI index of less than 10%. One subject in this group (12 months after delivery) showed a LH peak comparable to the peak at the time of ovulation in normally menstruating women. However, this was not followed by menses (Graph—III).

Discussion

Association of amenorrhoea and anovulation during the lactation period has been well documented. However, the physiological basis is not yet clear. Forbes (1954), Keettel and Bradbury (1961) Kellar (1968), Johnson and Fuchs in their reports postulated that a general suppression of ovarian response to gonadotrophins during lactation would be one of the factors for the lactational amenorrhoea. Zarate *et al,* (1973) attempted to define the activity of the ovaries during the postpartum period, did not observe any significant increase in urinary hormones in lactating patients receiving gonadotrophins after parturition. This he interpreted as due to a period of ovarian refractoriness which associated with a relatively delayed recovery of the pituitary gonadotrophin activity during lactation.

In our small series of lactational amenorrhoea patients, FSH values correspond to the FSH values in the follicular phase of normally menstruating women. LH values also correspond to the LH values in the normally menstruating women except that a peak of LH was noted in only one patient (12 months after delivery) which was comparable to the peak at the time of ovulation.

Faiman *et al,* (1968) Saxena *et al,* (1968) evaluating lactating postpartum patients also reported normal follicular

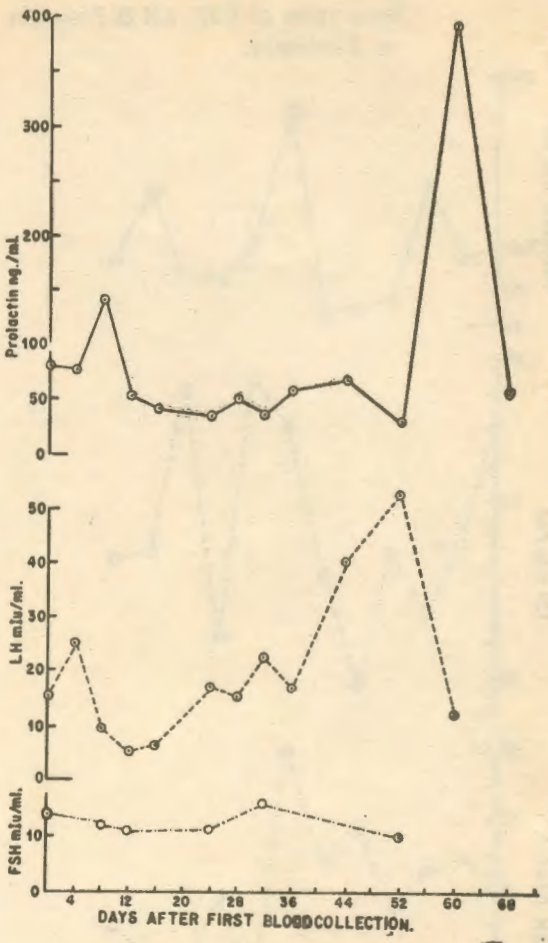

Fig. 3
Mean values of FSH. LH and prolactin in a woman with lactational amenorrhoea of one year.

phase levels of FSH and LH at 6 weeks postpartum in both lactating and non-lactating subjects. On the other hand, Crystle and Stevens (1969) and Hanson *et al,* (1970) found FSH levels approximately 25% of those detected during normal menstrual cycle. Keettel and Bradbury (1961) observed three types of excretion patterns of gonadotrophins. They are (i) levels as high as mid-intervals of the normal cycle (ii) intermittent excretion of gonadotrophins and (iii) un-

detectable gonadotrophins in 17% of patients.

Different trends of FSH and LH concentrations following parturition suggested the possibility that different regulatory mechanisms are operative or that the same stimulus elicits a different response by the pituitary, in the production of these two hormones Jaffe *et al,* (1969, 1973).

The close relationship between suckling and prolactin secretion was recognised experimentally long ago. Whether prolactin plays any role in inhibiting pituitary release of the gonadotrophins in the puerperium is not clearly known. The recent studies of Jaffe *et al,* (1969, 1973), Tyson *et al,* (1972) indicated an association of elevated prolactin levels and decreased gonadotrophins during lactating period. On the basis of their findings Tyson *et al,* have suggested that during the anovulatory phase of the puerperium, prolactin may have a blocking effect on gonadotrophins within the ovary. Reyes *et al,* (1972) who presented similar data, postulated that during lactation prolactin may antagonize the action of gonadotrophins at the level of the ovary. The results in the present study, also showed an increase in prolactin levels in 6 lactating patients out of 9. However, the baseline of prolactin levels had a wide range with numerous peaks. Tyson *et al,* (1972) and Jaffe *et al,* (1969, 1973) who also observed wide fluctuations in the prolactin levels explained that the unstable levels in the lactating subjects could be due to the intensity of the suckling stimulus Grosvenor et al, (1967). The decreased prolactin levels in two patients and a normal pattern in one patient in the present series appears to be analogous to the poor lactation of these subjects. Lactation in the puerperium requires prolactin, as patients with an isolated deficiency of prolactin are unable to lactate and nurse their infants Turkington (1972). However, Friesen (1971) felt that prolactin is not the only hormone responsible for lactation, since elevated levels are occasionally present in the absence of lactation.

Keettel and Bradbury (1961) found intermediate cornification in 50% of smears taken 4th to 12th postpartum months from women with lactational amenorrhoea, the rest were mature. All their patients had well cornified smears prior to the onset of menstruation. The atrophic vaginal smear frequently observed may be a reflection of the sluggish return of the ovary to menstrual cycle steroidogenic activity Crystle *et al,* (1970).

In conclusion, although the number of cases in the present study is small, the results suggest that ovarian refractoriness as a possible cause of amenorrhoea in these lactating mothers and thus supports the suggestions made by Keller (1968) and Zarate *et al,* (1972).

Summary

1. Serial estimation was done for FSH, LH and prolactin in 9 women with postpartum lactational amenorrhoea.

2. The levels of FSH and LH corresponded to the levels in follicular phase of the cycle in normally menstruating women.

3. Only one patient had LH peak similar to the LH peak at the time of ovulation in normally menstruating women, and this was not followed by menstruation.

4. Vaginal cytology whenever studied showed either atrophic or hypotrophic vaginal smears.

5. The study does indicate ovarian

refractoriness as a cause of lactational amenorrhoea.

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